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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/285,292	04/02/1999	DONNA G. ALBERTSON	023070-09140	3543

22798 7590 05/04/2004

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/04/2004

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/285,292	ALBERTSON ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Request for Continued Examination

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 18, 2004 has been entered.

2. Claims 1-17 are pending.

Claims 18-32 have been cancelled.

Claims 1-17 are examined on the merits.

Withdrawn Rejection

Claim Rejections - 35 USC § 112

3. The rejection of claims 18-32 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in light of the cancellation of claims.

New Grounds of Rejection and Objection

Specification

4. The title is not reflective of the claimed invention, which is a method of detecting CYP24.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' claims are directed to a method of prognosticating cancer by detecting the level of CYP24 by several means, such as comparative genomic hybridization (CGH) and detection of CYP24 mRNA. The written description is not commensurate in scope with these method claims drawn to CYP24, which have not been adequately described nor evidenced to be in the possession of Applicants. There is no corresponding sequence identifier, nor is it clear from the claims that there is only one sequence of the candidate cancer marker. Information provided in the specification sets forth "'*CYP24* gene' is a DNA sequence that encodes a 24-hydroxylase enzyme...The term gene can refer to a mutated copy of the gene, or a fragment of the gene", see page 7, lines 10-12. It follows that the acronym *CYP24* encompasses a genus of molecules, such as nucleic acids, proteins and mRNA that are not necessarily wild type forms of the *CYP24*. The term reads on a plethora of variant, mutated and alternate forms of CYP24. Applicants are not in possession of the entire genus of

CYP24 molecules embraced by the claim language. "Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identify characteristics sufficient to show that the applicant was in possession of the claimed invention", see Official Gazette, 1242 OG 172, January 30, 2001.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

The skilled artisan cannot envision the detailed structure of either BF-14 or BPI-14 and conception is not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The product itself is required. Applicants have not described CYP24 with sufficient particularity such that one skilled in the art would recognize that the Applicants had possession of the claimed invention. It is not clear from the instant application was filed that there was only one human

sequence of CYP24. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement, which defines a genus of nucleic acids by only their functional activity, does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

7. Claims 1-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants' claims are directed to a method of detecting a predisposition to cancer in an animal comprising the assessment of CYP24 levels in a biological sample. The broad term "cancer" encompasses several organ systems with different and distinct histopathologies and various etiologic causative agents. And more specifically, the term cancer reads on breast cancer. The prior art has reported genes amplified at 20q13.2, particularly the approximate 1-Mb region in breast cancer. However, CYP24 has been excluded as a candidate breast cancer gene, see Collins et al. Proc. Natl. Acad. Sci. USA 95: 8703-8708, July 1998/ IDS reference AI. The claims read on an embodiment that is not enabled. In essence, the breadth of the methodology claimed is not commensurate with the scope of the claims. There is insufficient guidance in the specification providing methodology consistent with the claims. Applicants' specification outlines detection of the level of CYP24 by measuring the level of CYP24 mRNA in human breast cancer cell lines and tumors with and without induction by 1,25 - dihydroxyvitamin D_3 evaluated by RT-PCR. Applicants' Figure 3 provides evidence that mRNA corresponding to CYP24 and vitamin D receptor (VDR) from human breast tumor cell lines can be detected, see page 18, lines 3-9; page 53, lines 15-27; and page 58, lines 5-7. In essence there is PCR amplification of specific CYP24 target RNA from either total RNA or mRNA. However, normal control data is not of record, hence one of ordinary skill in the art could not definitely assess whether or not the said method could lead one to detect the predisposition to any cancer including breast cancer in light of the data provided and the prior art of record that seems contrary to what Applicants assert.

There would need to be some valid amount of direction or guidance, as well as presence or absence of working examples presented in the specification that would enable one skilled in the art to perform the method as presented in the recited claims. It appears that undue experimentation would be required of one skilled in the art to practice the instant claimed invention using the teachings of the specification. See Ex parte Forman, 230 USPQ 546 BPAI, 1986.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "CYP24" in claims 1, 2, 9-11 and 15-17 are vague and indefinite. It is not clear what type of CYP24 molecule Applicants are referencing. Accordingly the metes and bounds are not clear.

b. Claim 6 is indefinite in the use of the recitations, "CYP24 mRNA" and "CYP24 RNA". The claim initially sets forth measuring the level of CYP24 mRNA and later requires the assessment of CYP24 RNA. The claim in itself is not further limiting, but rather broadens the scope of CYP24 and the claim language is not consistent.

c. Claims 7 and 10 are vague and indefinite because as written it is suggest that vitamin D receptor activity is equivalent or correlative to CYP24 mRNA and CYP24 protein. The activity and the mRNA or protein of CYP24 seem to require two different

modes of measurement and the assessment of one would not seem to be equivocal to the assessment of the other.

d. Claim 15 is vague and indefinite in the recitation "statistically significant difference". It is not clear what qualitative difference between CYP24 in the biological sample versus the CYP24 in the control sample is regarded as significant. Applicants do note in the specification that there are several sources that teach how to assess statistical significance this statement does not lend to what is regarded as significant in the instant case, see page 14, lines 17-22.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
3 May 2004